

WHAT IS CLAIMED IS:

Sub  
C-7  
✓ 1. An article of manufacture for human pharmaceutical use comprising:

(a) an oral dosage form comprising a PDE5 inhibitor having an  $IC_{50}$  for the inhibition of PDE5 less than 10 nM, and sufficient bioavailability to be effective in about 1 to about 10 mg unit oral dosages;

(b) a package insert providing that the PDE5 inhibitor is useful to treat sexual dysfunction in a patient in need thereof by utilizing a chronic dosing regimen; and

(c) a container.

✓ 2. An article of manufacture for human pharmaceutical use comprising:

(a) an oral dosage form comprising a PDE5 inhibitor having an  $IC_{50}$  less than 10 nM, and a sufficient bioavailability to be effective in about 1 to about 10 mg unit oral dosages;

(b) a package insert providing that the PDE5 inhibitor is useful to treat sexual dysfunction in a patient in need thereof by utilizing a chronic dosing regimen, wherein the chronic dosing regimen improves vaseular conditioning; and

(c) a container.

✓ 3. An article of manufacture for human pharmaceutical use comprising:

(a) an oral dosage form comprising a PDE5 inhibitor having an  $IC_{50}$  less than 10 nM, and a sufficient bioavailability to be effective in about 1 to about 10 mg unit oral dosages;

(b) a package insert providing that the PDE5 inhibitor is useful to treat sexual dysfunction in a patient in need thereof by utilizing a chronic dosing regimen, wherein the chronic dosing regimen improves vascular conditioning compared to an acute or on-demand dosing of sildenafil; and

(c) a container.

✓ 4. An article of manufacture for human pharmaceutical use comprising:

(a) an oral dosage form comprising a PDE5 inhibitor having an  $IC_{50}$  less than 10 nM, and a sufficient bioavailability to be effective in about 1 to about 10 mg unit oral dosages;

(b) a package insert providing that the PDE5 inhibitor is useful to treat sexual dysfunction in a patient in need thereof by utilizing a chronic dosing regimen, wherein the chronic dosing regimen improves vascular conditioning compared to an acute or on-demand dosing of vardenafil; and

(c) a container.

5. The article of manufacture of claims 1 through 4, wherein the PDE5 inhibitor further has

(i) at least a 100 fold differential in  $IC_{50}$  values for the inhibition of PDE5 versus PDE6, and

(ii) at least 1000 fold differential in  $IC_{50}$  values for the inhibition of PDE5 versus PDE1c.

✓ 6. The article of claims 1 through 4 wherein the oral dosage form comprises about 1 mg, about 2 mg, about 5 mg, or about 10 mg, of the PDE5 inhibitor.

✓ 7. The article of claims 1 through 4 wherein the chronic dosing regimen is a daily dosing regimen.

✓ 8. The article of claims 1 through 4 wherein the chronic dosing regimen comprises administration of about 1 mg/day to about 10 mg/day of the PDE5 inhibitor.

✓ 9. The article of claims 1 through 4 wherein the package insert provides a maximum dosage of the PDE5 inhibitor of about 10 mg per day.

10. The article of claims 1 through 4 wherein the PDE5 inhibitor is selected from the group consisting of

(6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione;

(3S,6R,12aR)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]-pyrido[3,4-b]indole-1,4-dione;

5-(2-ethoxy-5-morpholinoacetylphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-(5-morpholinoacetyl-2-n-propoxyphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-[2-allyloxy-5-(4-methyl-1-piperazinylsulphonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-{2-ethoxy-5-[4-(2-propyl)-1-piperazinylsulphonyl]phenyl}-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-{2-ethoxy-5-[4-(2-hydroxyethyl)-1-piperazinylsulphonyl]phenyl}-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-{5-[4-(2-hydroxyethyl)-1-piperazinylsulphonyl]-2-n-propoxyphenyl}-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

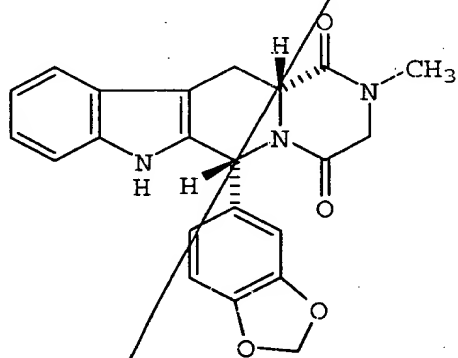
5-[2-ethoxy-5-(4-methyl-1-piperazinylcarbonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; and

5-[2-ethoxy-5-(1-methyl-2-imidazolyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one.

11. The article of claim 10 wherein the chronic dosing regimen comprises administration of about 1 mg/day to about 10 mg/day of the PDE5 inhibitor.

12. The article of claims 1 through 4 wherein the PDE5 inhibitor is selected from the group consisting of sildenafil and vardenafil.

13. The article of claims 1 through 4, wherein the PDE5 inhibitor has the structure



14. A method of treating sexual dysfunction comprising using an article of manufacture of claims 1 through 4.

15. A method of treating sexual dysfunction comprising a chronic administration to an individual in need thereof of one or more oral dosage form of a PDE5 inhibitor in an amount of about 1 mg/day to about 10 mg/day for at least three days.

16. The method of claim 15 wherein the chronic administration of a PDE5 inhibitor is a daily administration.

17. A method of improving a relaxant response in corpus cavernosum smooth muscle comprising a chronic administration of a PDE5 inhibitor selected from (6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]-pyrido[3,4-b]indole-1,4-dione for at least three days.

18. The method of claim 17 comprising the chronic administration of about 1 mg/day to about 10 mg/day of the PDE5 inhibitor.

add B3

add C1